### REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted in response to the Official Action dated March 6, 2007. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due consideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

#### Status of the Claims

Claims 10-11 and 13-14 are under consideration in this application. Claims 10-11 and 13-14 are being amended, as set forth in the above marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicant's invention. All the amendments to the claims are supported by the specification. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

#### Formality Rejection

The Examiner rejected claims 10, 11, 13 and 14 under 35 U.S.C. §112, first paragraph, as containing new matter. Further, the Examiner rejected claims 13 and 14 under 35 U.S.C. §112, second paragraph, as being indefinite, and specifically for language that was found to be indefinite and confusing. As outlined above, the claims are being amended to correct formal errors and/or to better recite or describe the features of the present invention as claimed in accordance with the Examiner's requirements.

In addition, Applicants will point out that the present invention as now claimed is fully supported in the disclosure of the invention, and that no recitation in the claims constitutes new matter. Specifically, claim 10 as amended recites a plurality of amphibian oocytes wherein relative to a Z-axis direction and an animal hemisphere of each amphibian oocyte being positioned in an upward direction relative to a vegetal hemisphere, each of the amphibian oocytes has mRNA positioned in a cytoplasm thereof at a depth relative to the Z-axis direction in the range of 0.02-0.1 mm from a top surface of the animal hemisphere of each of the amphibian oocytes, wherein the mRNA is injected into the cytoplasm of each of the plurality of amphibian oocytes.

Claim 13 as amended recites a method for screening a sample, comprising the steps of: injecting, relative to a Z-axis direction and an animal hemisphere of each of a plurality of

amphibian oocytes being positioned in an upward direction relative to a vegetal hemisphere, mRNA into a cytoplasm of each of the plurality of amphibian oocytes such that the mRNA in each of the plurality of amphibian oocytes is positioned at a depth relative to the Z-axis direction in the range of 0.02-0.1 mm from a top surface of each of the oocytes; maintaining a membrane potential on each of the oocytes injected with the mRNA; adding a solution to each of the oocytes maintained with the membrane potential, the mRNA being selected as a sample to encode a protein for initiating an interaction with the solution; and measuring an electric response of each of the oocytes after the step of adding thereby discriminating whether the solution is interacting the sample based on the electric response.

Support for the recitations of claims 10 and 13 may be found throughout the specification wherein "relative to a Z-axis direction" is supported on page 9, lines 2-20 ("At this point, the injection needle moving table 4 is operated by an indication of the control unit I for moving the injection needle to the direction of Z-axis, a tip of the injection needle 6 mounted on the injection unit 5 moves downward to the position slightly distant from the surface of the oocyte, for example, close to the front by several hundred mm. At this point, by observing the image taken by CCD camera 7 in the monitor 3, indication is given from the auxiliary control unit 2, and the injection needle moving table 4, operated to descending direction slowly. The contact of the tip of the injection needle 6 with the surface of the oocyte 13 can be detected by visual information, pressure changes, temperature changes, electric changes, moisture changes, or pH changes, then the injection needle moving table 4 is stopped at this position. This position is a reference point for the subsequent gene injection operation. This point is made to memorize in the control unit 1 and the following operation is performed. Namely, moving distance and depth of the injection needle for the vertical direction against a plane of the tray from the above reference point to the position of injecting sample are set, and the injection needle 6 is stuck at the setting depth to inject the previously fixed amount of the sample. For the injection of sample, a control for Z-axis direction can be performed, for example, such like that the injection needle moves downwardly to 0.2 mm from the contact point of the injection needle 6 on the surface of oocyte 13.").

Support for the recitation "an animal hemisphere of each amphibian oocyte being positioned in an upward direction relative to a vegetal hemisphere" may be found on page 7, lines 12-17 ("Consequently, by designing a diameter of well in the tray to be slightly larger than that of the oocytes in use, about 80% of the oocytes in average can be maintained to

keep their animal hemispheres upside, without changing the directions of oocytes arranged on the tray by rotating the cells, and the injection probability to the identical hemispherical surface can be increased up without using any other special means.").

Similarly, support for the recitations of claims 11 and 14 may be found throughout the specification wherein "an injection area substantially identical to an injection area in all others of the oocytes" is supported by page 11, lines 12-15 ("By using of the apparatus having the above constitution, the sample can be injected into the specific area and depth of the amphibian oocytes, and the oocytes which have almost same quality of the expression efficiency of the injected sample (injection efficiency), can be produced rapidly in mass production.").

Also, the recitation in claim 13 of "adding a solution to each of the oocytes maintained with the membrane potential, the mRNA being selected as a sample to encode a protein for initiating an interaction with said solution; and measuring an electric response of each of the oocytes after the step of adding thereby discriminating whether the solution is interacting said sample based on the electric response" is supported on page 14 line 20 to page 21, line 10 ("Histamine receptor gene 31 is injected into the oocyte 13 by using the apparatus assembled with the above constitution or using the above principles. In FIG. 6, the injection into the vegetal hemisphere is shown. After injection of histamine receptor gene, histamine receptor 32 is expressed in the oocytes 13 within 24 hours. As the same as in the above, after passing 24 hours from histamine receptor gene injection, membrane potential of the oocytes, in which histamine receptor 32 may be expressed, is held at -60 mV by two electrodes voltage clamp method. Under such conditions, addition of sample 33 containing histamine to the oocytes 13 results in interaction between histamines in the sample and histamine receptors, and the signal transduction system in the oocyte is activated to generate ionic current, then the electric response 34 of oocyte 13 against histamine can be shown. In case that sample 35 without histamine is added, since no substance, which interacts with the receptor, exists, the oocyte 13 can not respond to histamine 36. . . The oocyte expressed histamine receptor response against histamine containing samples can be used as the indicator. Since mass production of oocytes having identical condition for injection of the sample can be possible by using the apparatus for sample injection of the present invention, the amphibian oocytes can be used for screening of the ligand or antigen reacting with receptor or antibody. The screening can be performed by using plurality of oocytes, in which sample such as gene is injected under the substantially equal condition and protein or other

substances is expressed, and comparing the result of reactions of oocytes with defferent ligands.").

In view of the above citations from the specification, Applicants will submit that the recitations of the claims are fully supported and thus do not introduce any new matter in to the application. Accordingly, the withdrawal of the outstanding informality rejections is in order, and is therefore respectfully solicited.

## Prior Art Rejections

The Examiner then rejected claims 10, 11, 13 and 14 under 35 U.S.C. §102(b) as being anticipated by Brown (US Patent No. 5,688,938). Applicants have reviewed this rejection and hereby respectfully traverse.

The present invention as recited in claim 10 is directed to a plurality of amphibian oocytes wherein relative to a <u>Z-axis direction</u> and an animal hemisphere of each amphibian oocyte being positioned in an upward direction <u>relative to a vegetal hemisphere</u>, each of the amphibian oocytes has mRNA positioned in a cytoplasm thereof at a depth relative to the <u>Z-axis direction</u> in the range of 0.02-0.1 mm from a top surface of the animal hemisphere of each of the amphibian oocytes, wherein the mRNA is injected into the cytoplasm of each of the plurality of amphibian oocytes.

As recited in claim 13, the present invention is directed to a method for screening a sample, comprising the steps of: injecting, relative to a Z-axis direction and an animal hemisphere of each of a plurality of amphibian oocytes being positioned in an upward direction relative to a vegetal hemisphere, mRNA into a cytoplasm of each of the plurality of amphibian oocytes such that the mRNA in each of the plurality of amphibian oocytes is positioned at a depth relative to the Z-axis direction in the range of 0.02-0.1 mm from a top surface of each of the oocytes; maintaining a membrane potential on each of the oocytes injected with the mRNA; adding a solution to each of the oocytes maintained with the membrane potential, the mRNA being selected as a sample to encode a protein for initiating an interaction with the solution; and measuring an electric response of each of the oocytes after the step of adding thereby discriminating whether the solution is interacting the sample based on the electric response.

In contrast to the present invention, Brown merely injects mRNA into the vegetal pole (col. 51, lines 28-29) of the oocytes, wherein a 35 mm culture dish with a patch of nylon stocking fixed to the bottom is used to secure the oocytes. This reference does not disclose,

teach or suggest any structure or process for obtaining a plurality of amphibian oocytes into which mRNA is injected into each oocyte as recited in the claims.

As such, Brown fails to teach or suggest each and every feature of the present invention as recited in at least independent claims 10 and 13. As such, the present invention as now claimed is distinguishable and thereby allowable over the prior art cited in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

## Double Patenting Rejection

Lastly, the Examiner rejected claims 10 and 11 under the judicially-created doctrine of obviousness-type double-patenting on the grounds that the claims are unpatentable in view of claims 14-16, 18, 21, 24 and 26-27 of US Patent No. 6,593,129, and in view of claims 12-16 of US Application No. 10/876.551.

Attached herewith is a duly-executed Terminal Disclaimer with respect to the abovenoted conflicting patent, which hereby obviates this rejection. Applicants intend to intentionally abandon US Application 10/876,551, thereby also obviating the respective double patenting rejection.

# Conclusion

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicant's undersigned representative at the address and telephone number indicated below.

Respectfully submitted,

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